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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/925,140	08/08/2001	Preeti Lal	PF-0512-1 DIV	3400

27904 7590 04/13/2004

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EXAMINER	
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ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 04/13/2004

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 20030114

Application Number: 09/925,140
Filing Date: August 08, 2001
Appellant(s): LAL ET AL.

Barrie D. Greene
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 10/22/03.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct. The amendment after final filed 10/27/03 has been entered as indicated in the advisory action mailed 1/2/04.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The appellant's statement of the issues in the brief is correct.

(7) Grouping of Claims

The Brief states that all the claims are grouped together.

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

Reiger et al., Glossary of Genetics and Cytogenetics, Classical Molecular, 4th ED., Springer-Verlay, Berlin, 1976

Burgess et al, Journal of Cell Biology Vol 111 November 1990 2129-2138

Lazar et al Molecular and Cellular Biology Mar 1988 Vol 8 No 3 1247-1252

Schwartz et al, Proc Natl Acad Sci USA Vol 84:6408-6411, 1987

Lin et al Biochemistry USA Vol 14:1559-1563, 1975

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claim:

ISSUE 1

Claims 3-7, 9, 11, and 12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered have been summarizes as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence of absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art and the breadth of the claims. *Ex Parte Forman*, 230 USPQ 546 (BPAI 1986) and *In re Wands*, 858 F.2d731, 8 USPQ 2d 1400 (Fed. Cir. 1988).

The claims are broadly drawn to an isolated a polynucleotide that encodes a sequence comprising a naturally occurring amino acid that is at least 90% sequence

identical to SEQ ID NO:1, a naturally occurring variant at least 90% identical to SEQ ID NO:2, and methods of producing such.

The specification teaches SEQ ID NO: 1 (SDHH). SDHH is alleged to be a human serine dehydratase homolog. The properties of SDHH were determined by comparing the sequence of SDHH with rat and human liver dehydratase. The specification only mentions that SDHH has 56.7% identity with human liver dehydratase and also shares a potential casein kinase II phosphorylation site and two potential protein kinase C phosphorylation sites and analysis of these sequences in various libraries shows 48% of these sequences are associated with cancer, 29% are involved in immune response, and 23% are fetal, cell line or proliferating (see pages 14). A mere factor of similarity between sequences of the does not predict the activity of the protein and even a small difference between sequences could render substantial differences between the activities of the proteins.

In addition, the specification does not teach any other "naturally occurring" amino acid sequence that is at least 90% identical to SEQ ID NO:1 which would have the activity of SEQ ID NO:1.

Claim 3(b) and claim 9(b) are broadly drawn to a polynucleotide which encodes a polypeptide comprising a naturally-occurring amino acid sequence having at least 90% sequence identity to the amino acid sequence of SEQ ID No:1 and a method of producing such, however, the specification does not enable any amino acid sequence other than SEQ ID NO:1. The specification provides an activity for SEQ ID NO:1, however the claims in parts 3(b) and 9(b) do not require this activity. Therefore, one

skilled in the art would not reasonably know how to use naturally occurring sequences that are 90% identical to SEQ ID NO:1. Therefore, even a small difference between sequences could render substantial differences between the activities of the proteins. This is demonstrated below.

Protein chemistry is probably one of the most unpredictable areas of biotechnology. For example, the replacement of a single lysine at position 118 of the acidic fibroblast growth factor by a glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological activity of the protein (see Burgess et al, Journal of Cell Biology Vol 111 November 1990 2129-2138). In transforming growth factor alpha, replacement of aspartic acid at position 47 with asparagine, did not affect biological activity while the replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen (see Lazar et al Molecular and Cellular Biology Mar 1988 Vol 8 No 3 1247-1252).

Replacement of the histidine at position 10 of the B-chain of human insulin with aspartic acid converts the molecule into a superagonist with 5 times the activity of nature human insulin. Schwartz et al, Proc Natl Acad Sci USA Vol 84:6408-6411 (1987). Removal of the amino terminal histidine of glucagon substantially decreases the ability of the molecule to bind to its receptor and activate adenylate cyclase. Lin et al Biochemistry USA Vol 14:1559-1563 (1975). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification, will often dramatically affect the biological activity of the protein.

Thus, one skill in the art would realize that a sequence that is 90% identical to SEQ ID NO:1 would not necessarily have the activity of SEQ ID NO:1 and therefore would not function as SEQ ID NO:1. In addition, one skill in the art would know that polynucleotides that are 90% identical to SEQ ID NO:2 would not necessarily encode SEQ ID NO:1 and function as SEQ ID NO:1.

In view of the lack of predictability in the art, lack of guidance, and lack of examples, one skilled in the art would be forced into undue experimentation in order to practice the broadly claimed invention.

Response to Argument

It is noted that the parts of the rejection directed to "serine hydratase" activity (responded to in page 4, part A. in the Brief) is moot in view of the amendments to the claims in the amendment after final submitted 10/27/03 which has been entered.

Appellants argue on page 5 of the Brief that the claims are to polynucleotides not to the polypeptides they encode and therefore it is the polynucleotides that are relevant and one skill in the art would recognize that whether or not the polynucleotide encoded an SDHH protein having enzymatic activity, the use if the polynucleotide would be the same.

In response to this argument, claim 3 clearly is directed to a polynucleotide as stated in the Brief, but the claim requires the polynucleotide to encode a polypeptide. Thus, arguments presented by the examiner with respect to the polypeptide is relevant to the issue. The responses of record, including the Brief did not address the

unpredictability in the art of protein chemistry as stated in the rejection. It is clear that that one could determine a polynucleotide that encoded a polypeptide that is 90% identical to SEQ ID NO:1 and produce such, however the issue is whether one would know how to use such or polynucleotides that are 90% and naturally occurring to SEQ ID NO:2 because the polynucleotide does not encode a polypeptide with the activity of SEQ ID NO:1. Therefore how would one use the polynucleotide.

Appellants argue on page 6 of the Brief that methods of using polynucleotides such as those encoding SDHH are well known in the art and one of ordinary skill in the art would know how to use the claimed polynucleotide variants encoding SDHH polypeptides with or without enzymatic activity.

In response to this argument, the claims in parts 3(b), 9(b) and 11(b) do not require an activity or even encode SDHH, therefore, while it is correct that one would know how to use polypeptides that encode SDHH polypeptides, the claims do not require this function and this is at issue.

Appellants argue on pages 6-8 that the polynucleotides are useful in toxicology testing and microarray technology and state on page 8 that "one skill in the art, upon reading this specification, would know how to use the claimed SDHH-encoding polynucleotides".

In response to this, while the use in microarray and toxicology testing is acknowledged, the claims do not require that the polynucleotides encode a polypeptide with serine dehydratase activity and therefore one skill in the art would not know how to use the claimed polynucleotides. One skill in the art would not know how to use such

polynucleotides in microarrays or toxicology testing because the specification does not teach a disease or activity associated with the polynucleotides that are 90% identical. Thus, it is not a target for drug development, toxicology studies, or disease diagnosis. Significant further research would have to be conducted to identify disease states which correlate with altered levels or forms of the claimed polynucleotides and thus one skill in the art would not know how to use such.

ISSUE 2

Claims 3, 6-7, 9, 11-12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to polynucleotides encoding polypeptides which are naturally occurring with 90% identity to SEQ ID NO:1 or 90% identical to SEQ ID NO:2.

With the exception of SEQ ID NO:1 and SEQ ID NO:2 the specification does not teach any other naturally occurring sequences that have serine dehydratase activity . The claims also encompass naturally occurring amino acids that are 90% identical to SEQ ID NO:1 or SEQ ID NO:2, however, the specification only discloses SEQ ID NO:1 and SEQ ID NO:2 and no other variants.

The general knowledge in the art concerning variants does not provide any indication of how the structure of one variant is representative of unknown variants.

Reiger et al. (Glossary of Genetics and Cytogenetics, Classical and Molecular, 4th Ed., Springer-Verlay, Berlin, 1976) clearly define alleles as one of two or more alternative forms of a gene occupying the same locus on a particular chromosome... and differing from other alleles of that locus at one or more mutational sites (page 17). Thus, the structure of naturally occurring sequences are not defined. With the exception of SEQ ID NO:1 and SEQ ID NO:2 the skilled artisan cannot envision the detailed structure of the encompassed polynucleotides and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation.

Thus, one of skill in the art would not understand that the applicant had possession of the claimed invention at the time the instant application was filed.

Response to Arguments

It is noted that the parts of the rejection directed to "serine hydratase" activity (responded to in page 8-9 in the Brief) is moot in view of the amendments to the claims in the amendment after final submitted 10/27/03 which has been entered.

Appellants argue on pages 10-12 that the specification provides adequate written description of the claimed polynucleotide variants and states that SEQ ID NO:1 and 2 are disclosed and the specification describes variants that are 90% identical to SEQ ID NO:1 and 2. The response further states that the claimed variants are "naturally occurring" and as such the scope of the claimed variants are narrowed to a finite set. The response further states that the specification provides guidance in determining

percent identity and thus one skill in the art would recognize a polynucleotide variant having 90% identity to SEQ ID NO:1 or a polynucleotide encoding SEQ ID NO:1.

In response to this argument, while the specification does recite variants can be 90% identical, there is no such species disclosed except SEQ ID NO:1 and 2. In addition, while one can screen for polynucleotides that are 90% identical, this rejection is based on written description/possession not enablement. Appellants specification does not describe the structures of a "naturally occurring" variant or what such would look like.

Appellants argue on page 12-14 that the claims specifically define the claimed genus through the recitation of chemical structure and cites case law for such (see page 12-14).

In response to this the board will comment on the case law.

Appellants argue on page 14-15 that the present claims do not define a genus which is "highly variant" and argues that Brenner et al determined that 30% identity is a reliable threshold for establishing homology between sequences aligned over at least 150 residues and in accordance with Brenner et al naturally occurring molecules may exist which can be characterized as serine dehydratases which have as little as 30% identity over 150 residues to SEQ ID NO:1.

In response to this argument, again the claims, 3(b), 9(b), and 11(b), do not recite that the polynucleotide encodes SEQ ID NO:1 or has any activity related to serine dehydratase activity. While Brenner et al does state that as little as 30% may be reliable for assessing function, the issue is whether appellants were in possession of

"naturally occurring" variants. As such the Brief states that naturally occurring molecules "may" exist which could be characterized as serine dehydratases and thus, admits that it is unclear if they would. Therefore, how could appellants be in possession of such molecules if it is not known if they do exist.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

LARRY R. HELMS, PH.D
PRIMARY EXAMINER

Larry R. Helms
January 15, 2004

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